

147 Rec'd PCT/PTO 16 FEB 2006

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| <b>FILING BY "EXPRESS MAIL" UNDER 37 CFR 1.10</b>   |  |
| <b>EV 731064291 US</b><br>Express Mail Label Number | <b>February 16 2006</b><br>Date of Deposit |

|   |  |  |                                    |
|---|--|--|------------------------------------|
| Form PTO-1390-MOD<br>(REV 10-96)  |  | U. S. Department of Commerce Patent and Trademark Office             | ATTORNEY'S DOCKET NUMBER<br>333233 |
| <b>TRANSMITTAL LETTER TO THE UNITED STATES<br/>DESIGNATED/ELECTED OFFICE (DO/EO/US)<br/>CONCERNING A FILING UNDER 35 U.S.C. 371</b> |  | U.S. APPLICATION NO. (If known, see 37 CFR 1.5)<br><b>10/1568637</b> |                                    |
| INTERNATIONAL APPLICATION NO.<br>PCT/EP2004/009368  | INTERNATIONAL FILING DATE<br>20 August 2004 (20.08.04) | PRIORITY DATE CLAIMED<br>22 August 2003 (22.08.03)                   |                                    |
| TITLE OF INVENTION<br><b>INHIBITION OF S6 KINASE ACTIVITY FOR THE TREATMENT OF INSULIN RESISTANCE</b>                               |  |  |                                    |
| APPLICANT(S) FOR DO/EO/US<br><b>AUWERX ET AL.</b>   |  |  |                                    |

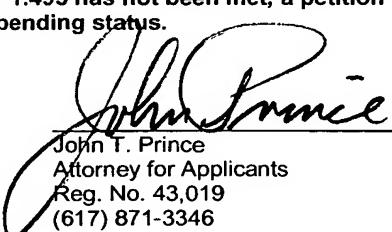
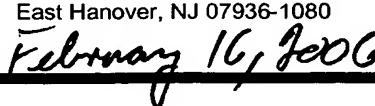
Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1.  This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2.  This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3.  This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4.  A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5.  A copy of the International Application as filed (35 U.S.C. 371(c)(2))
  - a.  is transmitted herewith (required only if not transmitted by the International Bureau).
  - b.  has been transmitted by the International Bureau. (See Form PCT/IB/308)
  - c.  is not required, as the application was filed in the United States Receiving Office (RO/US).
6.  A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7.  Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)).
  - a.  are transmitted herewith (required only if not transmitted by the International Bureau).
  - b.  have been transmitted by the International Bureau.
  - c.  have not been made; however, the time limit for making such amendments has NOT expired.
  - d.  have not been made and will not be made.
8.  A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)).
9.  An executed Declaration and Power of Attorney (original or copy) (35 U.S.C. 371(c)(4)).
10.  A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

**Items 11. to 16. below concern document(s) or information included.**

11.  An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12.  An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13.  A **FIRST** preliminary amendment.  
 A **SECOND** or **SUBSEQUENT** preliminary amendment.
14.  An Application Data Sheet under 37 CFR 1.76.
15.  A substitute specification.
16.  A change of power of attorney and/or address letter.
17.  A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 37 CFR 1.821-1.825.
18.  A second copy of the published International Application under 35 U.S.C. 154(d)(4).
19.  A second copy of the English language translation of the International application under 35 U.S.C. 154(d)(4).
20.  Other items or information: unexecuted Declaration; postcard

IAP20 Rec'd PCT/PTO 16 FEB 2006

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| U.S. APPLICATION NO. (if known, see 37 CFR 1.5)<br>101027   |              | INTERNATIONAL APPLICATION NO.<br>PCT/EP2004/009368   | ATTORNEY'S DOCKET NUMBER<br>333233 |
| The following fees are submitted:   |              | CALCULATIONS PTO USE ONLY  |                                    |
| 21. <input checked="" type="checkbox"/> Basic national fee: .....   |              | \$300  |                                    |
| 22. Examination Fee   |              |  |                                    |
| <input type="checkbox"/> If International preliminary examination report was prepared by USPTO and all claims satisfy provisions of PCT Article 33(1)-(4) .....   |              | \$   |                                    |
| <input checked="" type="checkbox"/> All other situations. ....  |              | \$200  |                                    |
| 23. Search fee  |              |  |                                    |
| <input type="checkbox"/> If Search fee (37 CFR 1.445(a)(2)) has been paid on the international application to the USPTO as an International Searching Authority. ....   |              | \$   |                                    |
| <input checked="" type="checkbox"/> If International Search Report was prepared and provided to the Office... ....  |              | \$400  |                                    |
| <input type="checkbox"/> All other situations. ....   |              | \$   |                                    |
| TOTAL OF 21, 22 AND 23 =  |              | \$ 900   |                                    |
| Additional fee for specification and drawings filed in paper over 100 sheets (excluding sequence listing or computer program listing filed in an electronic medium). The fee is \$250 for each additional 50 sheets of paper or fraction thereof.   |              |  |                                    |
| Total Sheets  | Extra sheets | Number of each additional 50 or fraction thereof (round up to a whole number)  | RATE                               |
| 41 - 100 =  | /50 =        | 0  | X \$ 250 \$                        |
| Surcharge of \$130 for furnishing the oath of declaration later than <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(e)).  |              |  |                                    |
| CLAIMS  | NUMBER FILED | NUMBER EXTRA   | RATE                               |
| Total claims  | 21           | - 20 = 1   | X \$ 50 \$ 50                      |
| Independent claims  | 5            | - 3 = 2  | X \$ 200 \$ 400                    |
| MULTIPLE DEPENDENT CLAIM(S) (if applicable)   |              | + \$ 360   | \$                                 |
| TOTAL OF ABOVE CALCULATIONS =   |              | \$ 1,350   |                                    |
| Reduction of 1/2 for filing by small entity, if applicable. Verified Small Entity Statement must also be filed (Note 37 CFR 1.9, 1.27, 1.28).   |              |  |                                    |
| SUBTOTAL = \$ 1,350   |              |  |                                    |
| Processing fee of \$130 for furnishing the English translation later than <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(f)).   |              |  |                                    |
| + \$  |              |  |                                    |
| TOTAL NATIONAL FEE = \$ 1,350   |              |  |                                    |
| Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40 per property   |              |  |                                    |
| + \$  |              |  |                                    |
| TOTAL FEES ENCLOSED = \$ 1,350  |              |  |                                    |
|   |              |  | Amount to be: refunded \$          |
|   |              |  | charged \$                         |
| <p>a. <input type="checkbox"/> A check in the amount of \$ _____ to cover the above fees is enclosed.</p> <p>b. <input checked="" type="checkbox"/> Please charge Deposit Account No. 19-0134 in the name of Novartis in the amount of \$1,350 to cover the above fees. A duplicate copy of this form is enclosed.</p> <p>c. <input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 19-0134 in the name of Novartis.</p> |              |  |                                    |
| NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.   |              |  |                                    |
| Send all correspondence to the address associated with Customer No. 001095, which is currently:   |              |  |                                    |
| Novartis<br>Corporate Intellectual Property<br>One Health Plaza, Building 104<br>East Hanover, NJ 07936-1080  |              | <br>John T. Prince<br>Attorney for Applicants<br>Reg. No. 43,019<br>(617) 871-3346 |                                    |
| <br>February 16, 2006  |              |  |                                    |